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Attorney Reference Number 4239-56113  
Application Number 09/676,718

Claim 55 was amended due to the cancellation of claim 25 and the election, and to change the percent identity. Support can be found on page 6, lines 32-37.

Claim 60 was amended due to the cancellation of claim 29.

Support for the new claims can be found throughout the specification, for example:

Claim 66: page 2, lines 20-23;

Claims 67-68: page 3, lines 9-12 and page 18, line 21 – page 19, line 9;

Claim 69: page 19, lines 7-9;

Claims 70-72: Claims 6 and 9; page 3, line 14; page 35 lines 30-34; and page 36,

lines 6-17;

Claims 73-77: page 7, line 32- page 8 line 16;

Claims 78 and 79: Claim 24 and page 36, line 36 – page 37, line 3;

Claim 80: Claim 26 and page 18, lines 18-20;

Claim 81: page 35, lines 30-34; and

Claim 82: page 17, table 2.

Certain groups that were restricted should be recombined, because SEQ ID NO: 4 is a subsequence of SEQ ID NO: 1 (amino acids 27-162 of SEQ ID NO: 1 are shown as SEQ ID NO: 4) and SEQ ID NO: 3 is a subsequence of SEQ ID NO: 2 (nucleotides 5-493 of SEQ ID NO: 2 are shown as SEQ ID NO: 3). Therefore, a search of SEQ ID NO: 1 will inherently result in a search of SEQ ID NO: 4, and a search of SEQ ID NO: 2 will inherently result in a search of SEQ ID NO: 3. Therefore, Applicants request that the following claim groups be combined:

Groups I and II (SEQ ID NOS: 1 and 4);

Groups IV and V (SEQ ID NOS: 1 and 4);

Groups VII and VIII (SEQ ID NOS: 1 and 4);

Groups X and XI (SEQ ID NOS: 2 and 3);

Groups XV and XVI (SEQ ID NOS: 2 and 3);

Groups XVIII and XIX (SEQ ID NOS: 1 and 4);

Groups XXI and XXII (SEQ ID NOS: 1 and 4);

Groups XXIV and XXV (SEQ ID NOS: 1 and 4);

Groups XXVII and XXVIII (SEQ ID NOS: 1 and 4);

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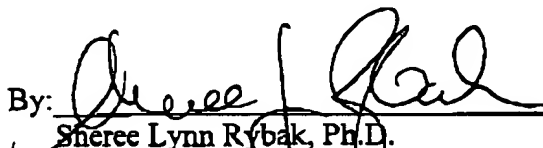
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Groups XXX and XXXI (SEQ ID NOS: 2 and 3);  
Groups XXXIII and XXXIV (SEQ ID NOS: 1 and 4);  
Groups XXXVI and XXXVII (SEQ ID NOS: 1 and 4);  
Groups XXXIX and XL (SEQ ID NOS: 1 and 4);  
Groups XLII and XLIII (SEQ ID NOS: 2 and 3);  
Groups XLV and XLVI (SEQ ID NOS: 1 and 4); and  
Groups XLVIII and XLIX (SEQ ID NOS: 1 and 4).

If the Examiner has any questions regarding this amendment and response to restriction requirement, he is invited to telephone the undersigned.

Respectfully submitted,

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**Marked-up Version of Amended Claims  
Pursuant to 37 C.F.R. §§ 1.121(b)-(c)**

1. (Cancel) [A purified peptide comprising at least 5 consecutive amino acids of an amino acid sequence selected from the group consisting of SEQ ID NOS: 1, 4, and 9.]
2. (Cancel) [A purified peptide according to claim 1 wherein the peptide comprises at least 10 consecutive amino acids of an amino acid sequence selected from the group consisting of SEQ ID NOS: 1 and 9.]
3. (Cancel) [A purified peptide according to claim 1 wherein the peptide comprises the amino acid sequence shown in SEQ ID NO: 1.]
4. (Cancel) [A purified peptide according to claim 1 wherein the peptide comprises the amino acid sequence shown in SEQ ID NO: 4.]
5. (Cancel) [A purified peptide according to claim 1 wherein the peptide comprises the amino acid sequence shown in SEQ ID NO: 9.]
6. (Cancel) [A specific binding agent that specifically binds to the peptide of claim 1.]
7. (Cancel) [A specific binding agent according to claim 6 wherein the specific binding agent is selected from the group consisting of polyclonal antibodies, monoclonal antibodies and immunologically active fragments of monoclonal antibodies.]
8. (Cancel) [A specific binding agent according to claim 6 wherein the specific binding agent is conjugated with a detectable label.]
9. (Cancel) [A method of quantifying the level of expression of a 15 kDa selenoprotein in a biological sample, the method comprising contacting the sample with a specific binding agent according to claim 6 under conditions whereby the specific binding agent forms a complex with any 15 kDa selenoprotein present, and quantifying said complexes.]
10. (Cancel) [A method of detecting the presence of a 15 kDa selenoprotein in a biological sample, the method comprising contacting the sample with a specific binding agent according to claim 6 under conditions whereby the specific binding agent forms a complex with any 15 kDa selenoprotein present, and detecting the presence of said complex.]
11. (Cancel) [A kit for detecting or quantifying a 15 kDa selenoprotein, the kit comprising a container containing a specific binding agent according to claim 6.]
12. (Cancel) [An isolated nucleic acid molecule that encodes the peptide of claim 1.]

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13. (Cancel) [The isolated nucleic acid molecule of claim 12, wherein the nucleic acid comprises a sequence selected from the sequences shown in the group consisting of SEQ ID NOS: 2, 3 and 8.]

14. (Cancel) [A recombinant nucleic acid vector including a nucleic acid sequence according to claim 13.]

15. (Cancel) [A transgenic cell produced by introducing into a cell a vector according to claim 14.]

16. (Cancel) [A method of generating the purified peptide encoded by the nucleic acid vector of claim 14 by introducing the vector into a cell and expressing the peptide from the cell.]

17. (Cancel) [The purified peptide of claim 16 wherein the peptide has an amino acid sequence selected from the sequences shown in the group consisting of SEQ ID NOS: 1 and 9.]

18. (Cancel) [A purified mammalian 15 kDa selenoprotein having at least 70% sequence identity to SEQ ID NOS: 1, 4, or 9.]

19. (Cancel) [A method of detecting the presence of a nucleic acid molecule that encodes the mammalian 15 kDa selenoprotein of claim 18 in a biological sample, comprising:

(a) contacting the sample with an oligonucleotide comprising at least 15 consecutive nucleotides of a sequence selected from the group consisting of SEQ ID NOS: 2 and 8 under conditions whereby said oligonucleotide will specifically hybridize to any nucleic acid molecule present in the sample that encodes the mammalian 15 kDa selenoprotein of claim 18; and

(b) detecting the presence of such hybridization.]

20. (Cancel) [A nucleic acid probe specifically hybridizable to a human 15 kDa selenoprotein RNA or cDNA.]

21. (Cancel) [A method of detecting a polymorphism in a human 15 kDa selenoprotein gene, comprising determining all or part of a nucleic acid sequence of the human 15 kDa selenoprotein gene, cDNA or mRNA in a biological sample.]

22. (Cancel) [The method of claim 21 wherein the polymorphism is C811/G1125.]

23. (Cancel) [A method of detecting a polymorphism in a human 15 kDa selenoprotein gene, cDNA or RNA in a biological sample, comprising hybridizing the sample with a nucleic acid probe under conditions whereby the probe will hybridize to the 15 kDa selenoprotein gene, or to cDNA or RNA carrying a polymorphism selected from the group consisting of C811, G1125 and C811/G1125, but not to a wild-type 15 kDa selenoprotein gene, cDNA or RNA.]

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24. (Cancel) [A method of detecting the mammalian 15 kDa selenoprotein of claim 18 in a cell, comprising administering to the cell <sup>75</sup>Se, and detecting <sup>75</sup>Se incorporated into a 15 kDa selenoprotein.]

25. (Cancel) [A method for dietary regulation, comprising detecting an abnormally low expression of the mammalian 15 kDa selenoprotein of claim 18 in a cell of a mammal and, if the level is reduced by at least 3-fold, enhancing the level by providing additional selenium in the diet of the mammal.]

26. (Cancel) [The method of claim 25 wherein the detection of the mammalian 15 kDa selenoprotein of claim 18 in the cell of the mammal is determined by a method selected from the group consisting of Western blotting of the mammalian 15 kDa selenoprotein of claim 18, Northern blotting of an mRNA coding for the mammalian 15 kDa selenoprotein of claim 18, and Southern blotting of a DNA encoding for the mammalian 15 kDa selenoprotein of claim 18.]

29. (Cancel) [A method for dietary regulation, comprising detecting a control level of the mammalian 15 kDa selenoprotein of claim 18 in a cell of a mammal, determining if the mammal is at an increased risk for cancers associated with defects in the mammalian 15 kDa selenoprotein of claim 18 and, if the risk is increased, decreasing the mammal's risk by providing additional selenium in the mammal's diet.]

30. (Cancel) [A method of determining a subject's susceptibility to developing cancer by determining a genotype of a mammalian 15 kDa selenoprotein gene in a sample from the subject comprising:

isolating DNA, cDNA, or mRNA from the sample;

amplifying the DNA, cDNA, or mRNA in a region containing a polymorphism at nucleotide positions 811 and 1125;

digesting the amplified DNA, cDNA or mRNA with restriction enzyme(s) which can distinguish the polymorphism by a differential restriction fragment length; and

detecting the polymorphism by the presence of the differential fragment length.]

31. (Cancel) [The method of claim 30 wherein the sample comprises a tumor cell.]

32. (Cancel) [The method of claim 30 wherein the sample comprises a normal cell.]

33. (Cancel) [The method of claim 30 wherein detecting the polymorphism comprises amplifying a DNA or cDNA of a mammalian 15 kDa selenoprotein gene with an amplification reaction using primers shown in SEQ ID NOS: 12 and 13.]

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34. (Cancel) [An oligonucleotide comprising a sequence selected from the group consisting of SEQ ID NOS: 12 and 13.]

36. (Cancel) [A method of determining a sequence of a polymorphism at positions 811 and 1125 of a mammalian 15 kDa selenoprotein gene by using the oligonucleotides of claim 34 to amplify a region containing the polymorphism.]

37. (Cancel) [A transgenic mouse which overexpresses [an] the isolated nucleic acid molecule of claim 12.]

38. (Cancel) [A transgenic mouse in which the nucleic acid molecule of claim 12 is functionally deleted.]

39. (Cancel) [A method of administering a therapeutically effective amount of the protein of claim 18 to a subject with an increased predetermined genetic susceptibility to cancer associated with a polymorphism in a 15 kDa selenoprotein gene having at least 70% sequence identity to SEQ ID NOS: 2, 3, or 8, wherein the protein of claim 18 is administered at a dose that reduces the subject's susceptibility to cancer.]

40. (Cancel) [The method of claim 39 wherein the protein is expressed by administering the recombinant nucleic acid vector of claim 14 into a subject with an increased predetermined genetic susceptibility to cancer associated with a polymorphism in a 15 kDa selenoprotein gene having at least 70% sequence identity to SEQ ID NOS: 2, 3, or 8, wherein expression of the recombinant nucleic acid in the subject provides a therapeutically effective amount of a 15 kDa selenoprotein having at least 70% sequence identity to SEQ ID NOS: 1, 4 or 9 to the subject.]

41. (Cancel) [A composition comprising a therapeutically effective amount of the protein of claim 18 and a pharmaceutically acceptable carrier.]

42. (Cancel) [The nucleic acid of claim 13, wherein the nucleic acid sequence has at least 70% sequence identity to SEQ ID NOS: 2, 3 or 8.]

43. (Cancel) [The nucleic acid of claim 13, wherein the nucleic acid sequence has at least 95% sequence identity to SEQ ID NOS: 2, 3 or 8.]

44. (Cancel) [The method of detecting a polymorphism of claim 21, wherein the nucleic acid sequence of the human 15 kDa selenoprotein gene has at least 70% sequence identity to SEQ ID NOS: 2, 3 or 8.]

45. (Cancel) [The method of detecting a polymorphism of claim 21, wherein the human 15 kDa selenoprotein gene has the nucleic acid sequence shown in SEQ ID NOS: 2, 3 or 8.]

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46. (Cancel) [A method of determining if a subject has an increased risk of developing cancers, comprising determining if there is a polymorphism in the subject's 15 kDa selenoprotein gene.]

47. (Cancel) [The method of claim 48, wherein the 15 kDa selenoprotein gene has at least 70% sequence identity to SEQ ID NOS: 2, 3 or 8.]

48. (Cancel) [The method of claim 48, wherein the polymorphism is selected from the group consisting of C811, G1125 and C811/G1125.]

49. (Cancel) [The method of claim 21, wherein detecting a polymorphism in a human 15 kDa selenoprotein gene is used to determine if a human has an increased risk of developing cancers.]

50. (Cancel) [The method of claim 23, wherein detecting a polymorphism in a human 15 kDa selenoprotein gene is used to determine if a human has an increased risk of developing cancers.]

51. (Amended) A method of determining if a subject has an increased risk of developing a cancer[s], comprising determining if [the] a cell of the subject has a[n abnormally low] reduced expression of [the purified] a mammalian 15 kDa selenoprotein having at least 70% sequence identity to SEQ ID NO: 1 or 4 [of claim 18 in the cells of the subject] when compared to expression of the 15 kDa selenoprotein in a control cell.

52. (Amended) The method of claim 51, wherein determining the reduced expression of the mammalian 15 kDa selenoprotein comprises determining whether the expression of the [purified] mammalian 15 kDa selenoprotein [of claim 18] is reduced by at least 3-fold in the cell of the subject when compared to expression of the 15 kDa selenoprotein in a control cell.

53. (Amended) The method of claim 51, wherein determining the reduced expression of the mammalian 15 kDa selenoprotein comprises determining whether the expression of the [purified] mammalian 15 kDa selenoprotein [of claim 18] is reduced by at least 50% in the cell of the subject when compared to expression of the 15 kDa selenoprotein in a control cell.

54. (Cancel) [A method for dietary regulation, comprising detecting an abnormally low expression level of the purified mammalian 15 kDa selenoprotein of claim 18 in a cell of a mammal and, if the level is reduced by at least 50%, enhancing the level by providing additional selenium in the diet of the mammal.]

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55. (Amended) The method of claim [25] 51, wherein the mammalian 15 kDa selenoprotein [of claim 18] has at least [95%] 90% sequence identity to SEQ ID NO[S]: 1[, 4, or 9] or 4.

56. (Cancel) [The method of claim 30, wherein the mammalian 15 kDa selenoprotein gene has at least 70% sequence identity to SEQ ID NOS: 2, 3 or 8.]

57. (Cancel) [The method of claim 36, wherein the mammalian 15 kDa selenoprotein gene has at least 70% sequence identity to SEQ ID NOS: 2, 3 or 8.]

58. (Cancel) [The transgenic mice of claim 37, wherein the nucleic acid molecule of claim 12 has at least 70% sequence identity to SEQ ID NOS: 2, 3 or 8.]

59. (Cancel) [The transgenic mice of claim 38, wherein the nucleic acid molecule of claim 12 has at least 70% sequence identity to SEQ ID NOS: 2, 3 or 8.]

60. (Amended) The method of claim [29] 51, wherein the cancer is selected from the group consisting of prostate cancer, liver cancer, head and neck cancers, and colon cancer.

61. (Cancel) [The method of claim 30, wherein the cancer is selected from the group consisting of prostate cancer, liver cancer, head and neck cancers, and colon cancer.]

62. (Cancel) [The method of claim 39, wherein the cancer is selected from the group consisting of prostate cancer, liver cancer, head and neck cancers, and colon cancer.]

63. (Amended) The [purified 15 kDa selenoprotein of claim 18] method of claim 51, wherein the 15 kDa selenoprotein has at least 95% sequence identity to SEQ ID NO[S]: 1[, 4, or 9] or 4.

64. (Amended) The [purified 15 kDa selenoprotein of claim 18] method of claim 51, wherein the 15 kDa selenoprotein comprises [the sequence shown in] SEQ ID NO[S]: 1[, 4, or 9] or 4.

65. (Cancel) [The method of claim 49, wherein the nucleic acid sequence is the nucleic acid sequence of claim 12.]

66. (New) The method of claim 51, wherein determining the reduced expression of the mammalian 15 kDa selenoprotein comprises determining whether the expression of the mammalian 15 kDa selenoprotein is reduced by at least 5-fold in the cell of the subject when compared to expression of the 15 kDa selenoprotein in a control cell.

67. (New) The method of claim 51, wherein the cancer is a prostate cancer.

68. (New) The method of claim 51, wherein the cancer is a liver cancer.

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69. (New) The method of claim 51, wherein the cancer is a lymphoma, ovarian cancer, or fallopian tube cancer.

70. (New) The method of claim 51, wherein determining expression of the mammalian 15 kDa selenoprotein comprises contacting a sample comprising the cell of the subject with a specific binding agent that specifically binds to the mammalian 15 kDa selenoprotein under conditions whereby the specific binding agent forms a complex with any 15 kDa selenoprotein present in the sample, and quantifying the complexes.

71. (New) The method of claim 70, wherein the sample is a biological fluid or a biopsy sample.

72. (New) The method of claim 71, wherein the biological fluid is blood.

73. (New) The method of claim 70, wherein the specific binding agent that specifically binds to the mammalian 15 kDa selenoprotein is an antibody.

74. (New) The method of claim 71, wherein the antibody is a polyclonal antibody.

75. (New) The method of claim 72, wherein the antibody is a monoclonal antibody.

76. (New) The method of claim 73, wherein the monoclonal antibody is a humanized monoclonal antibody.

77. (New) The method of claim 71, wherein the antibody is bound to a solid substrate.

78. (New) The method of claim 51, wherein determining expression of the mammalian 15 kDa selenoprotein comprises:

incubating  $^{75}\text{Se}$  with the cell of the subject; and

detecting  $^{75}\text{Se}$  incorporated into the mammalian 15 kDa selenoprotein.

79. (New) The method of claim 78, wherein incubating  $^{75}\text{Se}$  with the cell of the subject comprises administering the  $^{75}\text{Se}$  to the subject.

80. (New) The method of claim 51, wherein determining expression of the mammalian 15 kDa selenoprotein comprises Western blotting of the mammalian 15 kDa selenoprotein, Northern blotting of an mRNA coding for the mammalian 15 kDa selenoprotein, or Southern blotting of a DNA encoding for the mammalian 15 kDa selenoprotein.

81. (New) The method of claim 51, wherein the cell of the subject is a blood cell.

82. (New) The method of claim 51, wherein the cell of the subject is a thyroid or prostate cell.

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